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SUBTHERAPEUTIC USE OF ANTIBIOTICS IN ANIMAL FEED:
IN LIGHT OF AN UNRESOLVED CLASH OF EXPERT PARADIGMS
SHOULD WE PUNT TO THE CONSUMER IN DECADE FOUR?

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Food and Drug Law
Professor Hutt
February 2, 1998

A 'prudent use' of antibiotics is always recommended, but is difficult to apply.
French Researcher, Dr. E. Bergogne-Berezin, Participant, Symposium on
Antibiotic Resistance University of Southampton (July 12, 1996)

INTRODUCTION

In the early 1970s, the seemingly banal and nondescript matter of the subtherapeutic use of antibiotics in animal feed ignited a contentious debate in policy circles. For three decades now, this issue has periodically surfaced and resubmerged, each time provoking a heated but ultimately unresolved debate regarding the appropriate FDA regulation of the issue. FDA has on several instances taken initial action to find itself quickly restrained either by Congress or by its own ambiguous feelings on the issue. Today, different branches of the Public Health Service, the CDC and the FDA, hold strongly divergent views on this issue and even the Center for Veterinary Medicine, the Division of the FDA responsible for regulating the manufacture and distribution of animal feed additives, appears to house a range of opinion. *See infra* pp. 13-20.

Subtherapeutic use of antibiotics in animal feed, as opposed to therapeutic or disease-treating use, enhances efficiency of livestock production by promoting growth. Specifically, through an unknown mechanism, an animal on subtherapeutic doses of antibiotics will, on a lesser quantity of feed, gain an equal amount of weight as an untreated animal. *Animal Legal Defense Fund Boston, Inc. v. Provimi Veal Corporation*, 626 F.Supp. 278, 285-86 (D.Mass. 1986), *aff'd without opinion*, 802 F.2d 440 (1st Cir. 1987); Telephone Interview with Rich Carnevale, Vice President of Regulatory, Scientific and International Affairs, Animal Health Institute (January 29, 1998); Telephone Interview with Dr. Kathy Hollinger, Epidemiologist, Center for Veterinary Medicine, Food and Drug Administration (January 27, 1998). However, such efficiency gains are not without a cost. Subtherapeutic use of antibiotics poses some unknown level of risk of negative human health impacts by increasing the rate at which microbial

resistance accrues to clinically significant antibiotics. Some argue that the risk is too low to justify foregoing the economic benefits associated with the subtherapeutic regimens, while others argue that the risk is sufficient to justify a ban. An exploration of this debate and of a potential means for better accommodating the value conflict posed by this debate are the subject of this paper. Specifically, this paper will briefly discuss the history of the debate and then will discuss events leading to a recent reemergence of the issue. Next it will set forth the terrain of the dispute as it stands currently, and then finally will conclude by exploring the viability of labeling as a possible means of accommodating the divergent values invoked by the issue of subtherapeutic use of antibiotics in animal feed.

HISTORY

As the history of this issue has been aptly set forth by other authors, Peter Barton Hutt & Richard A. Merrill, *Food and Drug Law*, 646-655 (2d ed. 1991), this paper will only briefly summarize key historical developments.

As early as 1970, scientists within the U.S. and Britain began reviewing the issue of subtherapeutic use of antibiotics in animal feed. Both an FDA Task Force and a British Task Force, the Swann Committee, concluded that subtherapeutic use of antibiotics posed a potential hazard to human health and counseled conservative action. Antibiotic and Sulfonamide Drugs in Animal Feeds: Proposed Statement of Policy, 37 Fed. Reg. 2444 (1972); Peter Barton Hutt & Richard A. Merrill, *Food and Drug Law*, 646-649 (2d ed. 1991). In response to these findings, England proceeded to ban the subtherapeutic use of antibiotics in animal feed. Stuart B. Levy, *The Antibiotic Paradox: How Miracle Drugs are Destroying the Miracle* 141 (1992). The FDA indicated its concern about the issue and threatened to revoke existing approvals of uses of subtherapeutic uses of clinically significant antibiotics in feeds within two years unless data to establish their safety and effectiveness under the guidelines of the Task Force on the Use of Antibiotics in Animal Feeds guidelines were provided. Antibiotic and Sulfonamide

Drugs in Animal Feeds: Proposed Statement of Policy, 37 Fed. Reg. 2444 (1972); Peter Barton Hutt & Richard A. Merrill, *Food and Drug Law*, 647-649 (2d ed. 1991).

A little over a year after publishing this initial notice, FDA then took a step away from its earlier pronouncement. The Agency extended the deadlines before which data was required and set forth language suggesting that the potential risks posed by subtherapeutic use of antibiotics in feed had to be balanced against the benefits such policy provides. Antibiotic and Sulfonamide Drugs in the Feed of Animals, 38 Fed. Reg. 9811(1973). After pointing to the economic benefits which accrue from subtherapeutic use of antibiotics, FDA stated that proof of safety does not require complete certainty of the absolute harmlessness of a drug, but rather the reasonable certainty in the minds of competent scientists that it is not harmful when balanced against the benefits to be obtained from the drug. *Id* The agency further stated that withdrawal should be ordered only once a serious health hazard was demonstrated as it would be chaotic, and is clearly not feasible, to withdraw approval of all food or drug substances merely because new questions have arisen, new testing is considered scientifically appropriate, or new studies raise issues that require further exploration. *Id*

Winds of a second policy shift began to rustle in 1977 with the entrance of new Commissioner, Donald Kennedy. Peter Barton Hutt & Richard A. Merrill, *Food and Drug Law*, 650-651 (2d ed. 1991); *Antibiotics in Animal Feeds*, Center for Veterinary Medicine, Food and Drug Administration Web Page, <http://www.cvm.fda.gov/fda/infos/conl.html> FDA gave notice of its intent to propose rules to restrict subtherapeutic use of antibiotics in animal feeds and specifically proposing to ban subtherapeutic use of penicillin in feed and to restrict use of tetracycline to those situations in which there are no viable alternatives. Peter Barton Hutt & Richard A. Merrill, *Food and Drug Law*, 651-652 (2d ed. 1991). According to the FDA, penicillin and the tetracyclines were chosen because of their importance in the treatment of human disease. *Antibiotics in Animal Feeds*, Center for Veterinary Medicine, Food and Drug Administration Web Page, <http://www.cvm.fda.gov/fda/infos/>

consumer/conl.html.

Once again, however, FDA's move to restrict subtherapeutic antibiotics in animal feed was aborted. Congress, at the request of farm state legislators and the livestock and pharmaceutical industries, ordered the FDA to postpone its rule-making until additional data were gathered and considered. Barbara O'Brien, *Animal Welfare Reform and the Magic Bullet: The Use and Abuse of Subtherapeutic Doses of Antibiotics in Livestock*, 67 U. Cal. L. Rev. 407, 437 (1996). In retrospect, FDA writes that [t]he 1977 proposed withdrawals were criticized on the grounds that there was not adequate epidemiological evidence demonstrating that drug-resistant bacteria of animal origin are commonly transmitted to humans and cause serious illness. *Antibiotics in Animal Feeds*, Center for Veterinary Medicine, Food and Drug Administration Web Page, <http://www.cvm.fda.gov/fda/infos/consumer/conl.html>.

In 1978, Congress funded a National Academy of Sciences (NAS) analysis of the issue. The report produced by the NAS concluded that existing data had neither proved nor disproved the postulated hazards to human health from subtherapeutic microbial use in animal feeds and recommended a set of less expansive but more manageable analyses that could shed light upon some of the key issues in the debate. Peter Barton Hutt & Richard A. Merrill, *Food and Drug Law*, 652 (2d ed. 1991); *Antibiotics in Animal Feeds*, Center for Veterinary Medicine, Food and Drug Administration Web Page, <http://www.cvm.fda.gov/fda/infos/consumer/conl.html>

Three years later, Congress appropriated funds for an additional comprehensive study of the issue and again the House Appropriations Committee put FDA on notice that it should not move forward with the proposed withdrawal until the study was completed. *Antibiotics in Animal Feeds*, Center for Veterinary Medicine, Food and Drug Administration Web Page, <http://www.cvm.fda.gov/fda/infos/consumer/conl.html>. FDA selected the Seattle-King County Dept of Public Health to conduct the study and received the final report in August of 1984. *Id* Although FDA does not elaborate,

the agency was apparently not fully satisfied with the report, as they describe it merely by stating that the report has been accepted as having met contractual obligations. *Id*

Also in 1984, the Natural Resources Defense Council, Inc. (NRDC), petitioned Health and Human Services (HHS) for immediate suspension of approval of subtherapeutic use of penicillin and tetracyclines in animal feeds based on the imminent hazard provision of the Food, Drug and Cosmetic Act, 21 U.S.C. Sec. 360b(E)(1). *Id* Based on an analysis of the NRDC's evidence, evidence gathered at a public hearing and other relevant evidence, HHS Secretary Margaret Heckler denied the NRDC petition in late 1985, stating that an imminent hazard had not been established. *Id*.

In early 1989, the second weighty institutional review of the compiled evidence on this issue was released by the Institute of Medicine. Peter Barton Hutt & Richard A. Merrill, *Food and Drug Law*, 653 (2d ed. 1991). Like the NAS report a decade earlier, the IOM report stated that it was unable to find data directly implicating the subtherapeutic use of feed antimicrobials in human illness. Peter Barton Hutt & Richard A. Merrill, *Food and Drug Law*, 653 (2d ed. 1991) *citing Human Health Risks with the Subtherapeutic Use of Penicillin or Tetracyclines in Animal Feed* (1988). The report further remarked that much of the available evidence was primarily circumstantial, often ambiguous, and sometimes conflicting. *Id* According to an industry summary of the report, [s]cientists concluded that resistance to antibiotics was not solely a function of usage, but may result from the inevitable process of bacterial evolution. Other phenomena - including increased human resistance to antibiotics never used in animals and the prevalence of antibiotic resistance in developing countries where use of animal antibiotics is uncommon led the experts to conclude that human antibiotic resistance may be due to a variety of factors other than animal antibiotics. *Antibiotics in Animals*, The International Food Information Council Web Page, <http://ifinfo.health.org/insightlantibiot.htm>. The report set forth a new risk assessment model but stressed that its assumptions were based on an incomplete patchwork of data and that the model should be used only to help guide regulatory policy and should not be interpreted as a specific 'numerical

answer' about. .. human health risk. *Antibiotics in Animal Feeds*, Center for Veterinary Medicine, Food and Drug Administration Web Page, <http://www.cvm.fda.gov/fdaInfores/consu>

In the intervening decade, the FDA has continued to monitor this issue. According to the agency, FDA's Center for Veterinary Medicine has since the mid-80s completed an extensive literature review pertaining to all of the issues of science and health and has summarized scientific data from all completed contractual studies and articles printed in the scientific literature. *Id* The FDA position has been characterized by watchful concern but basic endorsement of standing policy. The FDA web page on the issue acknowledges existence of a risk, stating that [b]ecause these uses promote the development of drug resistant bacteria in animals, and routes for movement of these resistant bacteria to man are available, the Center believes that drug resistance in the bacteria associated with food animals can affect the proportion of drug resistant bacteria that cause human diseases. Therefore, the potential exists for compromise of drug therapy in animals and in humans. *Id* On the whole however, the agency finds the risk to be adequately balanced by countervailing benefits. In the words of CVM Director, Stephen Sundlof, [w]hile there are some risks associated with using antibiotics in animal agriculture, if managed properly, the benefits outweigh the risks. *Antibiotics in Animals*, The International Food Information Council Web Page, <http://ificinfo.health.org/insight/antibiot.htm>.

RECENT EVENTS REIGNITE THE DOMESTIC DEBATE

After a relatively sleepy period, recent events have brought a resurgence of interest and activity on the issue of subtherapeutic use of antibiotics. Events in the second half of 1997, decisive but controversial international action and domestic controversy over fluoroquinolones, gave rise to increased reflection both within and outside of FDA about the subtherapeutic use of antibiotics in animals. Telephone Interview with Rich Carnevale, Vice President of Regulatory, Scientific and International Affairs, Animal Health Institute (January 29, 1998). Telephone Interview with Fred Angulo,

Epidemiologist, Foodborne and Diarrheal Diseases Branch, Centers for Disease Prevention and Control (January 27, 1998).

INTERNATIONAL EVENTS

On October 17, 1997, the World Health Organization adopted a formal policy of opposition to the use of subtherapeutic levels of antibiotics in feed following a four day meeting of 70 international experts. *Antibiotic Use in Food-Producing Animals Must Be Curtailed to Prevent Increased Resistance in Humans*, World Health Organization Web Page, <http://wwwhq.who.or.jp/press/1997/pr97-73.html>. WHO stated that antibiotic use in food-producing animals must be curtailed to prevent increased resistance in humans. *Id.* [A]ntimicrobials are vital medicines to treat human infections but their effectiveness is threatened by overuse and inappropriate use which contributes to the growing resistance of bacteria. *Id.* In particular, the WHO stated that [r]esistant strains of... bacteria that cause disease in humans have been transferred from animals to humans and (have been) shown to have consequences for human health and pointed to existence of [d]irect evidence that antibiotic use in food-producing animals results in resistant... infections in humans. *Id.*

In addition to this policy announcement by the WHO, other significant international action also occurred. The Swedish, who have had a domestic ban on subtherapeutic use of antibiotics in animal feed since 1986, *Swedish Livestock Antibiotic Use Down Sharply*, Agra Europe, Nov. 8, 1996, launched a campaign to convince the E.U. of the wisdom of their position. Under the terms of its accession to the E.U., Sweden was granted a window of time in which it could retain its ban. *Swedes Push for Cuts in Antibiotic Use*, Agra Europe, Nov 14, 1997. That window, however, is fast elapsing and Sweden does not wish to have to relinquish their ban. *Id.* In the words of the Swedish Agriculture Minister, We would regard it as completely out of the question and unacceptable if we were required to alter our legislation in this time of growing awareness of the problem of antibiotics resistance.' *Id.* As part of its

campaign, the Swedish Ministry of Agriculture released a report stating that the risks of increased microbial resistance were more significant than the benefits of growth promotion. *Id.* The report, produced by the Swedish Commission on Antimicrobial Feed Additives (AFAs) stated that 'the risk of increased resistance associated with the general use of antibacterials as feed additives are far from negligible and the potential consequences are serious for both animal and human health.' *Id.*

A third significant action on the international front was the banning of the subtherapeutic use of the antibiotic avoparcin by the E.U. in response to current resistance concerns. *Id.*

Because of the potential relevance to these international experiences to our domestic debate, it is important to note that these international actions were based not on uncontroversial data but on a precautionary ethic. The WHO proceedings have been criticized as being one-sided and overly-dominated by those with an exclusive public health orientation. Telephone Interview with Sarah Lister, Congressional Aide, Senate Agriculture Committee Minority Staff (January 28, 1998). This critique is buttressed by the fact that the WHO statements themselves treat the economic considerations involved in a relatively dismissive and superficial manner. A decrease in use of antibiotics as growth promoters does not need to entail reduced productivity in animals and thereby economic losses to the food producer nor increased prices for (the) consumer. It will also not necessarily result in the increased use of other drugs in the place of antibiotics.. . Research on alternative methods to improve animal growth and feed efficiency was recommended. *Antibiotic Use in Food-Producing Animals Must Be Curtailed to Prevent Increased Resistance in Humans*, World Health Organization Web Page, <http://wwwhq.who.or.jp/press/1997/pr97-73.html>.

The action of the E.U. in banning avoparcin was also not without controversy. Leading up to the banning of avoparcin, UK made arguments similar to those employed in the U.S. The UK has argued that the ban on avoparcin, which is produced in the UK by Roche Pharmaceuticals, is not based on sound scientific evidence. . The UK is concerned that banning substances by referring to the

precautionary principle, i.e. without any prior evidence of harmful effect...could establish an unwelcome precedent.. . *EU Ban on Avoparcin Blocked; UK Commissioners Block Ban on Feed Additive*, *Agra Europe*, Jan 24, 1997. The scientific basis for the decision was also called into question by an independent scientific panel, the Scientific Commission of Animal Nutrition. J. Bates, *Review*:

Epidemiology of Vancomycin-Resistant Enterococci in the Community and the Relevance of Farm Animals to Human Infection, 37 *Journal of Hospital Infection* 89, 96-97 (1997). The Commission was asked to make an objective decision on behalf of the EU in answer to the question: 'Does the use of avoparcin constitute a danger to human health?' Although not unanimous, it was the committee's finding that there was at present insufficient evidence. *Id* In spite of this finding of insufficient evidence, the E.U. proceeded to impose a ban on the use of avoparcin in feed. *Id*. The decision, which has been described as being largely due to public pressure, is subject to review in two years. *Id*

FLUOROQUINOLONE DEBATE

The second factor causing a reawakening of the domestic debate over sub-therapeutic use of antibiotics in feed is the current debate over fluorquinolone policy. Telephone Interview with Rich Carnevale, Vice President of Regulatory, Scientific and International Affairs, Animal Health Institute (January 29, 1998); Telephone Interview with Fred Angulo, Epidemiologist, Foodborne and Diarrheal Diseases Branch, Centers for Disease Prevention and Control (January 27, 1998); Telephone Interview with Sarah Lister, Congressional Aide, Senate Agriculture Committee Minority Staff (January 28, 1998). Fluoroquinolones are significant because they are our current last line of defense against some bacteria. Telephone Interview with Fred Angulo, Epidemiologist, Foodborne and Diarrheal Diseases Branch, Centers for Disease Prevention and Control (January 27, 1998); Telephone Interview with Sarah Lister, Congressional Aide, Senate Agriculture Committee Minority Staff (January 28, 1998). Therapeutic use of fluorquinolones in poultry was approved by the FDA in 1995 and Bayer, the manufacturer of these

antibiotics, has recently sought FDA approval for use of fluoroquinolones in additional livestock. Marian Burros, *Health Concerns Mounting Over Bacteria in Chickens*, New York Times, Oct. 20, 1997 at A1. This request for expansion became quite controversial this fall when the NYT reported that campylobacter bacteria, a bacteria found on between 70 to 90% of all chickens, was found to be showing resistance to the fluoroquinolone class of antibiotics. *Id* Since the approval of the use of fluoroquinolones in poultry in 1995, the Minnesota Health Department had observed increased levels of drug resistant campylobacter in humans. *Id* According to the Department's random sampling in supermarkets, 79% of the chickens sampled were infected with campylobacter and of these, 20% had resistant strains. Of turkeys, 58% had campylobacter and 89% had resistant strains. *Id*. The data are being submitted to a scientific journal for publication. *Id* Similar results have been observed in a number of other countries. *Id*; *Antibiotic Use in Food-Producing Animals Must Be Curtailed to Prevent Increased Resistance in Humans*, World Health Organization Web Page, <http://wwwhq.who.or.jp/press/1997/pr97-73.htm> I.

Although the fluoroquinolone debate is about the appropriateness of therapeutic use of fluoroquinolones, the debate is raising the question of the appropriateness of subtherapeutic use of antibiotics also. Telephone Interview with Fred Angulo, Epidemiologist, Foodborne and Diarrheal Diseases Branch, Centers for Disease Prevention and Control (January 27, 1998). The reason is twofold. First, in the eyes of those who counsel conservative use of antibiotics, there is in practice a fine line between therapeutic use and subtherapeutic use. Telephone Interview with Kathy Hollinger, Epidemiologist, Center for Veterinary Medicine, FDA (January 27, 1998); Telephone Interview with Fred Angulo, Epidemiologist, Foodborne and Diarrheal Diseases Branch, Centers for Disease Prevention and Control (January 27, 1998). According to Hollinger, Right now there are a lot of drugs being abused.. . Most drugs we put out on the market are abused in some fashion. Telephone Interview with Kathy Hollinger, Epidemiologist, Center for Veterinary Medicine, FDA (January 27, 1998). Angulo and

Lister point out that the way antibiotics are applied therapeutically illustrates the fine line dividing the two categories. Telephone Interview with Kathy Hollinger, Epidemiologist, Center for Veterinary Medicine, FDA (January 27, 1998); Telephone Interview with Fred Angulo, Epidemiologist, Foodborne and Diarrheal Diseases Branch, Centers for Disease Prevention and Control (January 27, 1998). Fluorquinolones are apparently applied in drinking water. Telephone Interview with Sarah Lister, Congressional Aide, Senate Agriculture Committee Minority Staff (January 28, 1998); Telephone Interview with Fred Angulo, Epidemiologist, Foodborne and Diarrheal Diseases Branch, Centers for Disease Prevention and Control (January 27, 1998). Secondly, because fluoroquinolones are such important human clinical drugs, the debate highlights the whole issue of trade-offs between the benefits of efficiencies of livestock production and the potential risks to human health.

The future implications of these current events are difficult to determine. According to some commentators, the issue of antibiotic use is a very hot issue for the FDA right now, Telephone Interview with Fred Angulo, Epidemiologist, Foodborne and Diarrheal Diseases Branch, Centers for Disease Prevention and Control (January 27, 1998), causing the agency to do some soul-searching. Amanda Spake et al., *O is for Outbreaks*, U.S. News and World Report, November 24, 1997. However, this is certainly not the first time that predictions of imminent change have been made with regard to this issue. Barbara O'Brien, *Animal Welfare Reform and the Magic Bullet: The Use and Abuse of Subtherapeutic Doses of Antibiotics in Livestock*, 67 U. Cob. L. Rev. 407, 438 (1996). Others perceive the present as a periodic resurfacing of the same old issues. Telephone Interview with Jean Cooper, Veterinary Medical Officer, Center for Veterinary Medicine, FDA (January 28, 1998). Cooper reports that the issue comes and goes and that she doesn't see this time as different. *Id*

One means of attempting to determine how close these issues are to resolution is to examine the views of key players. The following section lays forth the basic terrain of the current debate.

PERSPECTIVES: THE EPIDIMIOLOGIST VS. THE RISK ASSESSER

This debate is centrally staked out by two camps¹, those with an epidimio-logical perspective and those with a risk assessment perspective. The following pages will lay out the arguments of both paradigms, citing significant players in the debate.

THE EPIDIMIOLOGISTS

The epidimiological perspective regards human health as the primary consideration in this debate. Examples of those holding this perspective include the CDC, the WHO and many physicians.

Because they privilege human health concerns, those with the epidimiological perspective tend to believe that any use which detracts from the potency of antibiotics for human medicine is highly suspect. In the words of Fred Angulo of the Centers for Disease Control and Prevention, CDC believes that antibiotics should be used prudently. Prudence is defined as use that maximizes the therapeutic effect and minimizes the emergence of resistance. Telephone Interview with Fred Angulo. Epidimiologist, Foodborne and Diarrheal Diseases Branch, Centers for Disease Prevention and Control (January 27, 1998). Since with antibiotics, the more you use them the faster you lose them, Patrick Wall, Chief of Gastrointestinal Disease, Public Health Service Laboratory, London *cited in* Amanda Spake et al., *O is for Outbreaks*, U.S. News and World Report, November 24, 1997, they see widespread and nonessential animal use as unacceptably eating away antibiotic potency that may mean fewer treatment options in human medicine. To give a sense of the magnitude of increased loss of resistance due to what they view as nonessential animal use, they point to the size of the market. Together,

The animal rights/animal welfare perspective constitutes a third basic position in the debate. This perspective more fundamentally critiques the efficiency-driven modern livestock production systems. As such a critique is beyond the scope of this paper, it will not be addressed here. For more information on this perspective, see Animal Welfare Reform and the Magic Bullet: The Use and Abuse of Subtherapeutic Doses of Antibiotics in Livestock, 67 UColo. L.Rev. 407 (1996) (arguing that the subtherapeutic antibiotics issue is a potential means of affecting broader issues of animal well-being).

subtherapeutic and therapeutic antibiotics used in farm animals equal half of the global antibiotic market. Vincent Perreten, et al., *Antibiotic Resistance Spread in Food*, 389 Nature 801 (1997). Of this market, the proportionate breakdown of subtherapeutic versus therapeutic use is difficult to pinpoint, but the subtherapeutic use is unquestionably significant. A well-known crusader for protection of our antibiotic reserves, Dr. Stuart Levy, has put the subtherapeutic figure at around 80%. Stuart B. Levy, *The Antibiotic Paradox: How Miracle Drugs are Destroying the Miracle* 140 (1992). A more conservative estimate might put the figure closer to 35%, the amount by which Sweden's total use of antibiotics in animals decreased after Sweden banned the subtherapeutic use of antibiotics. *Swedish Livestock Antibiotic Use Down Sharply*, Agra Europe, Nov 8, 1996. Whatever the exact statistics, given the importance of human health considerations, the view the collective data on risks presented by subtherapeutic use of antibiotics as presently sufficient grounds for a ban on the practice. *Antibiotic Use in Food-Producing Animals Must Be Curtailed to Prevent Increased Resistance in Humans*, World Health Organization Web Page, <http://wwwhq.who.or.jp/press/1997/pr97-73.html>. In the words of Congressional Aide Lister, The CDC and people who deal with public health see a lot of this stuff as a no brainer. Telephone Interview with Sarah Lister, Congressional Aide, Senate Agriculture Committee Minority Staff (January 28, 1998).

Those of the epidemiological perspective tend to view the FDA regulatory approach as inadequate, calling it worrisome. Telephone Interview with Fred Angulo, Epidemiologist, Foodborne and Diarrheal Diseases Branch, Centers for Disease Prevention and Control (January 27, 1998). The FDA approval process is not adequate to address the current issue... The legal mechanism doesn't take into account why society needs a drug... And if a drug is approved, a legal battle to get it off the market could take up to 10 years, at which point the utility of the drug has decreased to close to zero. That regulatory framework causes us in public health to be concerned. *Id.*

Those within the epidemiological paradigm also recommend prompt action to restrict

subtherapeutic use of penicillin and tetracycline, disagreeing with the claims of some that such restrictions would be too late to be effective. Telephone Interview with Kathy Hollinger, Epidemiologist, Center for Veterinary Medicine, FDA (January 27, 1998); Telephone Interview with Fred Angulo, Epidemiologist, Foodborne and Diarrheal Diseases Branch, Centers for Disease Prevention and Control (January 27, 1998). Describing the policy of the CDC, Angulo states [w]e support the WHO policy which says that use of certain classes of antibiotics should be terminated. We call for the termination of the subtherapeutic use of penicillin and tetracycline. Telephone Interview with Fred Angulo, Epidemiologist, Foodborne and Diarrheal Diseases Branch, Centers for Disease Prevention and Control (January 27, 1998). Both Angulo and Hollinger point to the resurgence in resistance experienced by Sweden after it reduced its antibiotic use in agriculture. Telephone Interview with Kathy Hollinger, Epidemiologist, Center for Veterinary Medicine, FDA (January 27, 1998); Telephone Interview with Fred Angulo, Epidemiologist, Foodborne and Diarrheal Diseases Branch, Centers for Disease Prevention and Control (January 27, 1998).

Believing strongly in precaution where public health is concerned, epidemiologists also tend to believe that fluoroquinolones, as our current last line of defense, should not be approved for use in animals even for restricted therapeutic use. Pointing to the fine line between subtherapeutic and therapeutic use, Angulo states that, We need to evaluate current approval of fluoroquinolones for therapeutic use for prudence. Telephone Interview with Fred Angulo, Epidemiologist, Foodborne and Diarrheal Diseases Branch, Centers for Disease Prevention and Control (January 27, 1998). According to Patty Leiderman of the Center for Science in the Public Interest, the current need to resort to fluoroquinolones in animal treatment results from the careless use of previous antibiotics and thus doesn't instill confidence that fluoroquinolones will be used responsibly. Telephone Conversation with Patty Leiderman, Center for Science in the Public Interest (January 27, 1998). Lister points out that in light of the recent Minnesota Health Department report regarding campylobacter resistance to fluoroquinolones

and the fact that such resistance developed so quickly (since 1995 approval of fluoroquinolones in poultry), we should be reticent with regard to future fluoroquinolone approvals. Telephone Interview with Sarah Lister, Congressional Aide, Senate Agriculture Committee Minority Staff (January 28, 1998). If we are going to lose this antibiotic 3 yrs after putting it out there, it is not worth it. *Id.*

At essence, the theoretical underpinning of the epidemiological perspective in the subtherapeutic use of antibiotic debate is a variant of the precautionary principle. According to Professor Cross, author of an article discussing and critiquing the precautionary principle, the first formulation of the precautionary principle was set forth by Talbot Page in 1978. Frank B. Cross, *Paradoxical Perils of the Precautionary Principle*, 53 Wash. & Lee L. Rev. 851, 852 (1996). In Cross's words, in the Page paradigm a false negative could cost lives, while a false positive, such as banning a truly harmless chemical, would have only economic consequences and probably minor ones at that. Given the asymmetry in the consequences of error, Page urged that we error on the side of preventing false negatives at the expense of some false positives. *Id.* This higher valuing of human health and life over potential economic consequences even at the expense of potential false positives is the basic underpinning of the general epidemiological disapproval of the subtherapeutic use of antibiotics in animal feed.

THE RISK REGULATORS

The alternate perspective in this debate is that of the risk regulator. Key proponents of this view include the FDA and members of industry. In this perspective, public health protection is a very important consideration but has to be balanced against other factors in the equation. Thus, consideration of what is forgone by imposing a given level of regulation as is quantification of the level of risk posed.

The risk regulator perspective either explicitly or implicitly considers benefits derived from tolerating current levels of risk. In the already quoted words of the present CVM Director, While there

are some risks associated with using antibiotics in animal agriculture, if managed properly, the benefits outweigh the risks. *Antibiotics in Animals*, The International Food Information Council Web Page, <http://ificinfo.health.org/insight/antibiot.htm>. While debate participants state that the exact levels of economic benefit are difficult to quantify, Rich Carnevale, Vice President of Regulatory, Scientific and International Affairs, Animal Health Institute (January 29, 1998), one estimate is that antibiotics allow a 2-3% gain in feed efficiency over what would occur without antibiotics. Telephone Interview with Jean Cooper, Veterinary Medical Officer, Center for Veterinary Medicine, FDA (January 28, 1998). Although this may sound insignificant, even slight efficiency gains translated over large numbers of animals become extremely important. Rich Carnevale, Vice President of Regulatory, Scientific and International Affairs, Animal Health Institute (January 29, 1998). In addition, if the practice were not resulting in efficiency gains, one would assume that producers would not purchase the antibiotics. Producers wouldn't do it unless it was profitable. Telephone Interview with Jean Cooper, Veterinary Medical Officer, Center for Veterinary Medicine, FDA (January 28, 1998). Specific statistics on the benefit to consumers of this efficiency gain are elusive. Rich Carnevale, Vice President of Regulatory, Scientific and International Affairs, Animal Health Institute (January 29, 1998). Nonetheless, based on global statistics, it is clear that U.S. consumers pay less for food than individuals in other countries. U.S. consumers have benefited from American food-production capabilities. Americans spend proportionately less on food, about 11 percent of their income, than do most residents of other parts of the world. In Europe, consumers spend about 14 percent of their income on food; in Japan, 21 percent; in China, about 48 percent. The percentage of income Americans spend on food has dropped by 50 percent since the turn of the century. *Backgrounder- Agriculture and Food Production*, International Food Information Council Web Page, <http://ificinfo.health.org/background/bkgr12.htm>.

Because countervailing benefits are tangible to them, risk regulators are unconvinced by vague assertions of potential scientific risks. According to Lister, public health assumes reasonable inferences

if no one has disproven them... But risk assessment says prove it. Telephone Interview with Sarah Lister, Congressional Aide, Senate Agriculture Committee Minority Staff (January 28, 1998). In Carnevale's words, millions have been spent looking at the issue: how big is the risk? The bottom line is that no one has been able to determine that the frequency of transmission is significant. Yes, it can happen but what is the impact? It is very difficult to conclude scientifically that there is a real risk. Rich Carnevale, Vice President of Regulatory, Scientific and International Affairs, Animal Health Institute (January 29, 1998). Cooper of FDA agrees and emphasizes that FDA has a different mandate than CDC. Telephone Interview with Jean Cooper, Veterinary Medical Officer, Center for Veterinary Medicine, FDA (January 28, 1998). She says that no one has definitively proven that resistance to antibiotics in an animal is going to result in impact on human health. The question is how often resistance is spread from a treated animal to a human pathogen. CDC says it is often enough to cause a problem but we have no proof. *Id* FDA has to strike the balance between potentially harming a few vs. potentially raising the cost of food. There are two sides of the debate: one says we may have a problem and the other says we have a problem. To the regulator, outliers on bell curve don't matter where as to the epidemiologist, every incident is an issue... FDA cares about risk assessment, about the general effect on the general public. We aren't guaranteeing zero risk. A lot of people don't understand that about how FDA works. We try to minimize the risk. There is no way to eliminate it. On this issue, we would take action if had more data, especially data on frequency. We have no good data, only soft surveillance data. *Id*.

Risk assessors acknowledge that through increased use we are likely accelerating the rate at which resistance accrues, but say that through careful controls we can attain the benefits of use while limiting loss of resistance. If you are using an antibiotic, you are going to get some resistance to it at some point. It is going to happen. The only question is the pace. You want to control how much occurs and make sure you don't create resistance unnecessarily. Telephone Interview with Rich Carnevale,

Vice President of Regulatory, Scientific and International Affairs, Animal Health Institute (January 29, 1998). To that end, risk assessors argue that the current system of case by case approval is adequate. We advocate carefully controlled use rather than banning. Johan Vanhemelrijk, Secretary General of the European Animal Health Federation (FEDESA) agrees. *Swedes Push for Cuts in Antibiotic Use*, Agra Europe, Nov. 14, 1997. 'We support a system of individual risk assessment based on scientific evaluation of the criteria of quality, safety and efficacy.' *Id* In addition, Carnevale points out that these products are highly regulated. Telephone Interview with Rich Carnevale, Vice President of Regulatory, Scientific and International Affairs, Animal Health Institute (January 29, 1998). FDA specifies the conditions for use of each drug in detail. *Id*. In addition to these regulatory controls, risk regulators point out that there are additional checks on antibiotic use because producers count on the effectiveness of antibiotics to treat sick animals and because these drugs are costly. *Id*

As to the issue of penicillin and tetracycline, risk regulators tend to argue that use of these drugs has decreased on its own and that many of the products used commonly in animals are not useful in human medicine. Telephone Interview with Rich Carnevale, Vice President of Regulatory, Scientific and International Affairs, Animal Health Institute (January 29, 1998); Telephone Interview with Jean Cooper, Veterinary Medical Officer, Center for Veterinary Medicine, FDA (January 28, 1998). As to the fluorquinolones, the risk regulator perspective once again favors controlled use over banning. They report that an FDA advisory committee studied the issue three years ago and reached the conclusion that there was a need for treatment with fluorquinolones and that it should be allowed under limited, veterinarian controlled therapeutic circumstances subject to post approval monitoring. Telephone Interview with Rich Carnevale, Vice President of Regulatory, Scientific and International Affairs, Animal Health Institute (January 29, 1998). Risk regulators tend to view that policy as the appropriate balancing of the factors involved. *Id*. In response to the NYT report that 20% of campylobacter chickens randomly sampled in Minnesota were fluoroquinolone resistant, the risk regulator perspective

again questions the data and the implied mechanism of action. National Broiler Council representative Kenneth May stated, We don't treat anything like 20% of chickens with fluorquinolones. Lisa Zimmerman, *Campylobacter News Not Affecting Sales; Bacteria Commonly Present In Raw Chicken*, Supermarket News, Nov. 3, 1997. National Broiler Council representative Roenigk, agreed, stating Less than 1/10 of 1% of chickens get treated with fluorquinolone. .. fluoroquinolone is 25 times more expensive [than other antibiotics]. *Id* Dean Cliver, a professor of food safety at U.C. Davis said that he was not worried about fluoroquinolone resistant campylobacter in humans because 'antibiotics are not recommended for treatment of campylobacter [in humans]. *Id*. Cliver said that the more important issue was people learning to handle raw chicken. *Id*

The theoretical underpinning of the risk regulator perspective is also set forth by Professor Cross. Frank B. Cross, *Paradoxical Perils of the Precautionary Principle*, 53 Wash. & Lee L. Rev. 851, 852 (1996). Cross critiques the precautionary principle by stating, among other things, that it skews prioritization of government efforts to reduce risk. The consequence is less risk reduction than would otherwise occur. *Id.* at 86 1-2. He proposes an alternative principle which is grounded in the limitations and uncertainties of scientific knowledge. While these limitations are undeniable, they do not call for an artificial decision rule that ignores the science, such as the precautionary principle. Rather, policymakers should confront the scientific uncertainty and act prudently in accord with the best possible scientific understanding. This approach may sometimes call for precaution, but only after considering the potentially substantial risks attendant to precaution. The proposed policy might itself be considered a form of the precautionary principle, though in vastly expanded form, with better recognition of the full consequences of regulatory action. *Id.*

IN THE FACE OF THIS ENTRENCHED VALUES-BASED DISAGREEMENT: SHOULD WE ALLOW THE CONSUMER TO CHOOSE?

The above sections set forth the two basic sides of this debate. Barring some catastrophic event, the future of this debate will likely bring continued fighting and thus continued supremacy of the risk regulator approach, despite existence of significant dissension. Given the current lack of consensus about the values-based dilemma presented by subtherapeutic use of antibiotics, the possibility of using a labeling mechanism to accomodate broader levels of choice and expression suggests itself. A labeling scheme would allow consumers to express their views on this values debate through the market, thus diminishing the hegemonic importance of the particular position adopted by the regulatory scheme.

In considering the labeling option, three questions need to be answered: 1) Would such a labeling scheme be legal? 2) Is such a labeling scheme desirable? and 3) Could it work?

LEGAL CONTEXT

Recent case law and FDA guidance indicate that non-misleading voluntary labeling by producers is permissible.

The Second Circuit recently declared unconstitutional a Vermont law requiring rBST (recombinant Bovine Somatotropin) labeling of dairy products, finding that Vermont had failed to assert a substantial state interest to justify its intrusion on constitutionally protected rights. *International Dairy Foods Ass '12 v. Amestoy*, 92 F.3d 67 (2nd Cir. 1996). The court left open the question of whether mandatory labeling could be acceptable in a case in which a substantial state interest was demonstrated. Absent..., some indication that this information bears on a reasonable concern for human health or safety or some other sufficiently substantial government concern, the manufactures cannot be compelled to disclose it. Instead, those consumers interested in such information should exercise the power of their purses by buying products from manufacturers who voluntarily reveal it. *Id* at 74. Future decisions

will help to resolve the balance to be struck regarding mandatory labeling, but in the meantime, it is safe to assume based on *International Dairy Foods* that voluntary labeling is permissible.

In addition, the FDA has issued potentially relevant guidance on the content of labels in the rBST context. Fredrick Degnan, *The Food Label and the Right-to-Know*, 52 Food & Drug L. J. 49, 55-59 (1997). Such guidance emphasize(s) that if voluntary labeling is to be employed, misleading implications must be avoided and that the information presented must appear in its proper context. *Id.* at 56. The agency has cautioned that even truthful information could mislead consumers. *Id.* In specific terms, [t]he interim guidance suggests that whenever a dairy product carries a label that reads from cows not treated with rBST, the label should also include the disclaimer that [n]o significant difference has been shown between milk derived from rBST-treated and non-rBST treated cows. Terence J. Centner & Kyle W. Lathrop, *Labeling rBST-Derived Milk Products: State Responses to Federal Law*, 45 Kansas L. Rev. 511, 523 (1997). While the presence of a legitimate scientific dispute may distinguish the subtherapeutic antibiotic case from the rBST case, even if the rBST guidance is applicable in its entirety to the subtherapeutic antibiotics case, it should not present a problem with thoughtful drafting.

To summarize, a voluntary, non-misleading labeling program for animal products raised without subtherapeutic use of antibiotics should not encounter legal stumbling blocks.

IS LABELING DESIRABLE [N A CASE SUCH AS THIS?

Two categories of argument suggest the desirability of labeling in the subtherapeutic antibiotic case: "information economics" arguments and consciousness raising" arguments.

Several powerful justifications for labeling are provided by the information economics approach. First, informational approaches to regulation enhance personal liberty by increasing the power of the individual to make free choices. .. Second, informational approaches increase economic efficiency by

providing information that consumers want, but because of some market failure, do not have. Third, informational approaches enhance democracy because they promote citizen participation in and debate over risk management. Michael Barsa, *California's Proposition 65 & the Limits of Information Economics*, 49 Stanford L. Rev. 1223, 1226-7 (1997) citing Cass. R. Sunstein, *Informing America: Risk, Disclosure and the First Amendment*, 20 Fla. St. U. L. Rev. 653, 655-58 (1993).

Second, labeling in the context of this debate may also provide the additional benefit of consciousness raising set forth by Barsa in his discussion of California's Proposition 65. Michael Barsa, *California's Proposition 65 & the Limits of Information Economics*, 49 Stanford L. Rev. 1223, 1238-1247 (1997). While on its face Proposition 65 seems to be all about informing consumers, it also supplies powerful incentives to manufacturers to become informed about and possibly reduce the carcinogens and teratogens in their products. *Id* at 1239. Barsa reports that Proposition 65 has encouraged industry to reduce the level of toxins or to keep toxins out of the market entirely to escape the warning requirements. *Id* at 1240. Although weaker within a voluntary labeling system, a consciousness raising effect would likely still occur in this case to some degree either because of producer desire to take advantage of a potentially significant market or possibly, in the future, to escape the stigma of not having a label. The incentive to alter production processes could become significant in time if the organic foods market is any indicator of the potential for market expansion. Since 1990, organic sales have skyrocketed at the rate of twenty percent per year, propelling organic food to the status of a legitimate food niche with annual sales between \$2.9 and \$3.3 billion. Kenneth C. Amaditz, *The Organic Foods Production Act of 1990 and its Impending Regulations: A Big Zero for Organic Food?*, 52 Food & Drug L. J. 537 (1997). The French experience also documents the potential of a significant market. The French have a system of meat labeling which occupies a substantial market segment. There are no fewer than 5300 Label Rouge poultry farmers in France, and they represent one third of the poultry sold in France. This is true even though the price premium for such products is

200-300%. Neil Murray, *Red Means Go; Free Range Chicken Market in the UK*, Frozen and Chilled Foods, August, 1997. Given this potential for future impact on production processes, the consciousness raising justification further supports the desirability of labeling in the subtherapeutic antibiotic context.

COULD IT WORK?

A voluntary labeling approach would appear to lead to the predicted benefits set forth by the information economics paradigm above. First, by providing the information necessary to distinguish products on the basis of subtherapeutic antibiotic use, a labeling approach will supply an incentive to raise animals without use of subtherapeutic antibiotics. This, in turn, will provide consumers a choice that was not present before initiation of the labeling scheme, enabling them to weigh the considerations involved on either side of the debate. Second, because such labeling would provide at least some consumers access to information that they deem relevant to their purchasing decisions but that they did not formerly have, a labeling approach would thus also increase market efficiency by reducing an information imperfection in the market. Third, labeling would also be likely to enhance democracy by informing consumers of the existence of this debate and by tabulating their votes on the matter through the market mechanism.

Critics would point to a number of potential downsides to the labeling approach. First, they would argue that it is actually not desirable to make risk regulation decisions more democratic given the reality of irrational public risk perception. Second, critics would question whether the public has the capacity to really understand a warning on the subtherapeutic antibiotic issue. They would point out that the debate is somewhat complex and technical and the language confusing. Third, critics would also point to the incompleteness of the information provided by such a labeling approach and ask why this issue is being privileged above other important issues. They would question whether it makes sense to begin the labeling enterprise given the impossibility of providing perfect labeling on all issues. Fourth,

critics would argue that if we start labeling to allow people to express their values, this will lead to an ever-expanding quantity of labels that will ultimately completely overwhelm consumers, rendering the entire labeling enterprise meaningless. Fifth, critics would argue that it is strange to have a labeling system in a premium is paid not to avoid a potential personal risk but a potential public risk.

Many of these concerns are surmountable. With respect to the first issue, the question of the desirability of democracy in regulation, the pro-labeling perspective would respond that popular input on regulatory decisions actually is desirable when scientific consensus is lacking and values questions are paramount.

As to the question of whether consumers can grasp the issues at stake, the pro-labeling perspective believes strongly that most consumers will definitely be able to comprehend this issue. Most individuals with access to mainstream media of any sort will already have significant grasp of the issues involved and will relatively quickly be able to absorb additional information and develop a personal opinion on the matter. Even in the worst case scenario, however, if only some individuals were able to understand and process the information, even that incremental increase in informed choice would be an enhancement over no choice at all.

Third, the labeling proponent would acknowledge both the incompleteness of the labeling exercise and its privileging of some issues over others. However, given that perfect decision-making is an impossibility, the labeling advocate would argue that the relevant question should be whether a given label has rendered decision-making less imperfect than it otherwise would have been. The labeling advocate believes that we should look for improvement not perfection. True, the information is still incomplete but if it is less incomplete than it otherwise would have been, the label has incrementally diminished the information imperfections of the market.

Fourth, the labeling advocate disputes the argument that labeling will result in an eventually crushing information load. The advocate points to the existence of built-in checks which will prevent

such an eventuality. Labels by nature only go on the relevant product - meat, fruit, etc, - not on all products. This in and of itself decreases the information load presented. In addition, consumers are not so easily overwhelmed by information as critics predict. Consumers don't conduct complex analyses on every product each time they enter a store but rather evolve decision-making efficiencies - operating paradigms that guide their behavior. The availability of labels can help to inform these operating paradigms by making information available to consumers in their environment. Consumers wishing not to attend to the information can easily tune it out. Making the information available to the consumer when possible allows each consumer to be the judge as to what matters to him or her. Lastly, if at some point in the future we are concerned that labels have become too unruly and overwhelming, we could through regulation establish a means of prioritization, privileging issues in which there is a genuine scientific dispute and in which values are paramount. We're far from that situation today, however.

Fifth, the labeling advocate would argue that although a labeling system in which a consumer pays a premium to minimize contribution to a societal risk is somewhat unusual, there is some precedent for such a system and there is no inherent reason that it is not defensible. Although many individuals purchase organic goods to minimize risks to their own health, some purchase organic goods based on broad societal concerns such as the desire to minimize the detrimental environmental impacts of pesticide-dependent agricultural production. Further, even if there were no such precedent, the fact that a benefit is a dispersed public benefit rather than a concentrated individual benefit does not appear to be a valid moral basis for not allowing the choice. If a consumer desires to pay more for meat in order to help to protect a societal good in an incremental fashion along with other consumers, the consumer should have the option of doing so.

To summarize, although it would be imperfect in many respects, a labeling system which would provide consumers the option of purchasing meat produced without subtherapeutic use of antibiotics could be a means of achieving increased levels of liberty, efficiency and democracy within the context of

a stalled public policy debate.

CONCLUSION

This paper has explored the clash of two dominant expert paradigms over the use of subtherapeutic antibiotics in animal feed. Given the apparent insolubility of this battle and the policy dominance of one side in the debate, a labeling scheme is one potential means of allowing greater levels of expression and choice in what is essentially a values-based debate.